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          E MANAGER D/AU
L1        1 S E6
          E HAO C/AU
L2       20 S E3-4,E10,E46,E52,E72
          E UNGER M/AU
L3       56 S E3-4,E19-20,E23
L4       59 S MICROFLUIDIC(7A)(POLYMER OR ELASTOM? OR FLEXIBLE)
L5       47 S (MICROFLUIDIC OR MICROMACHIN? OR MICRO(1A)(FLUIDIC OR MACHIN?))AND
            (ELECTROSPRAY OR(ELECTRO OR THERMO OR ION)(1A)SPRAY OR THERMOSPRAY OR
            IONSPRAY)
L6      172 S (MICROPLATE OR MICROCHIP OR PLATE OR CHIP)AND(ELECTROSPRAY OR
            (ELECTRO OR THERMO OR ION)(1A)SPRAY OR THERMOSPRAY OR IONSPRAY)
L7      329 S L1-6
L8      320 S L7 NOT(OYSTER OR BLUMEI OR CORRO?)
L9      309 S L8 NOT(SPINOSA OR MAGNETOOPT? OR SUPERCRYT? OR INDUCTION FURNACE)
L10     303 S L9 NOT(SCANNING PROBE OR CRUCIBLE OR BASED DEPOSITION)
L11     291 S L10 NOT(BREED? OR PINE OR NANOPARTICLE OR NANOMETER FE OR FINITE
            ELEMENT OR RURAL OR AIR POLLUTION)
L12     277 S L11 NOT(NMR OR CELL ADHESION OR AQUATIC OR ATOMIC FORCE)

=> d l12 bib,ab 1-277

L12  ANSWER 12 OF 277  CA  COPYRIGHT 2002 ACS
AN   136:17441  CA
TI   Miniaturized multichannel electrospray ionization emitters on
     poly(dimethylsiloxane) microfluidic devices
AU   Kim, Jin-Sung; Knapp, Daniel R.
CS   Department of Pharmacology, Medical University of South Carolina,
     Charleston, SC, 29425, USA
SO   Electrophoresis (2001), 22(18), 3993-3999
AB   A multichannel electrospray ionization (ESI) emitter was fabricated as part
     of a poly(dimethylsiloxane) (PDMS) microfluidic device using a three-layer
     photoresist process which also produces a self-alignment system to make a
     bonding between the top and bottom PDMS parts. The prototype device (2 cm
     high × 5 cm wide × 5 cm long) had 16-channels (30 μm wide × 50 μm deep)
     with emitters of 1 mm length and 60° point angle. The PDMS emitter tips
     enabled interfacing the device to ESI-mass spectrometry; a stable electro-
     spray from the tips was performed with limits of detection under 1 μM for
     ref. peptides (adrenocorticotropic hormone fragment 1-17, angiotensin I and
     III).

L12  ANSWER 15 OF 277  CA  COPYRIGHT 2002 ACS
AN   136:10982  CA
TI   Microstructures and micro-fluidics in polymers
AU   Geschke, Oliver; Rong, Weimin; Kutter, Joerg P.; Telleman, Pieter;
     Ostergaard, Steen; Tang, Peter T.
CS   Mikroelektronik Centret, Kgs Lyngby, Den.
SO   Medical Plastics 2000, Collected Papers of the International Conference,
     14th, Vienna, Austria, Sept. 11-14, 2000 (2000), 7.1-7.4. Editor(s): Skov,
     Hroar R. Publisher: Hexagon Holding ApS, Copenhagen, Den.
AB   A review, with refs., on the different fabrication processes of master
     tools for prepg. polymer microstructures. One of these processes is the
     micro-milling prototype, which offers fast access to simple microfluidic
     structures and rapid conversion of three-dimensional structure from a CAD
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10/15/2001

program to a polymer microstructure. Other processes include injection molding, back-end processes, and hot embossing, which is the preferred process for polymer microstructures.

L12 ANSWER 21 OF 277 CA COPYRIGHT 2002 ACS
AN 135:341015 CA
TI Microfabrication of polydimethylsiloxane electrospray ionization emitters
AU Kim, J.-S.; Knapp, D. R.
CS Department of Pharmacology, Medical University of South Carolina, Charleston, SC, 29425, USA
SO J. Chromatogr., A (2001), 924(1-2), 137-145
AB Microfabricated polydimethylsiloxane (PDMS) emitters for electrospray ionization mass spectrometry (ESI-MS) were implemented as tips along the edge of the PDMS device by three methods which utilize soft lithog. processes. These microfabrication methods for producing PDMS emitters as an integral part of a microfluidic device will facilitate development of more complex microfluidic anal. systems using ESI-MS.

L12 ANSWER 35 OF 277 CA COPYRIGHT 2002 ACS
AN 135:124442 CA
TI Separation media, multiple electrospray nozzle system and method
IN Corso, Thomas N.; Schultz, Gary A.; Prosser, Simon J.; Huang, Xian
PA Advanced Bioanalytical Services, Inc., USA
SO PCT Int. Appl., 146 pp.
PI WO 2001053819 A1 20010726 WO 2001-US1785 20010118
US 2002000517 A1 20020103 US 2001-764698 20010118
PRAI US 2000-176605P P 20000118
AB A microfabricated silicon chip with a sepn. material, such as in situ prepd. porous polymer monoliths in its microchannels is disclosed. The polymer monoliths are liq.-permeable and serve as microcolumns for liq. chromatog., which are prepd. by in situ radical polymn. of a mixt. contg. vinyl monomers and solvents (pyrogen) in the microchannels. A method and system are disclosed to generate one or more electrospray plumes from one or more nozzles that provide an ion intensity as measured by a mass spectrometer that is approx. proportional to the no. of electrospray plumes formed for analyses contained within the fluid. A plurality of electrospray devices can be used in the form of an array of miniaturized sep. electrospray devices for the purpose of generating multiple electrospray plumes from multiple nozzles for the same fluid for anal.

L12 ANSWER 41 OF 277 CA COPYRIGHT 2002 ACS
AN 135:58090 CA
TI High-throughput microfabricated CE/ESI-MS: Automated sampling from a microwell plate
AU Zhang, Bailin; Foret, Frantisek; Karger, Barry L.
CS Barnett Institute and Department of Chemistry, Northeastern University, Boston, MA, 02115, USA
SO Analytical Chemistry (2001), 73(11), 2675-2681
AB A new design for high-throughput microfabricated capillary electrophoresis/electrospray mass spectrometry (CE/ESI-MS) with automated sampling from a microwell plate is presented. The approach combines a sample-loading port, a sepn. channel, and a liq. junction, the latter for coupling the device to the MS with a miniaturized subatmospheric electrospray interface. The microdevice was attached to a polycarbonate manifold with external electrode reservoirs equipped for electrokinetic and pressure-fluid control. A computer-activated electropneumatic distributor was used for both sample loading from the microwell plate and washing of channels after each run. Removal of the electrodes and sample reservoirs

from the microdevice structure significantly simplified the chip design and eliminated the need both for drilling access holes and for sample/buffer reservoirs. The external manifold also allowed the use of relatively large reservoirs that are necessary for extended time operation of the system. Initial results using this microfabricated system for the automated CE/ESI-MS anal. of peptides and protein digests are presented.

L12 ANSWER 42 OF 277 CA COPYRIGHT 2002 ACS
AN 135:40184 CA
TI Integrated monolithic microfabricated electrospray and liquid chromatography system and method
IN Moon, James E.; Davis, Timothy J.; Galvin, Gregory J.
PA Kionix, Inc., USA
SO U.S., 56 pp.
PI US 6245227 B1 20010612 US 1998-156037 19980917
PRAI US 1998-156037 A3 19980917
AB Electrospray devices are described which comprise a silicon substrate having a first surface and a second surface; an entrance orifice defined on the first surface; a nozzle defined on the second surface; a channel extending between the entrance orifice and a tip of the nozzle; a recessed region surrounding the nozzle recessed from the second surface; at least one of the channel, entrance orifice, nozzle and recessed region being formed at least in part by reactive-ion etching; and an insulating layer provided over at least the interior surface of the channel and the interior and exterior surfaces of the nozzle to elec. isolate the surfaces from the substrate. Integrated miniaturized systems for electrospraying fluids comprising the devices and means for providing elec. potential with respect to ground to the fluids are also described. The systems may be integrated with a sepn. substrate (e.g., a liq. chromatog. system) defining an introduction channel between an entrance orifice and a reservoir and a sepn. channel between the reservoir and an exit orifice, the sepn. channel being populated with sepn. posts perpendicular to the fluid flow; a cover substrate bonded to the sepn. substrate to enclose the reservoir and the sepn. channel adjacent the cover substrate; and, optionally, electrode(s) for application of a elec. potential to the fluid. An array of multiple systems may be fabricated in a single monolithic chip for rapid sequential fluid processing and generation of electrospray for subsequent anal., such as by positioning the exit orifices of the electrospray devices near the sampling orifice of a mass spectrometer. Application to anal. in drug discovery and development is indicated.

L12 ANSWER 43 OF 277 CA COPYRIGHT 2002 ACS
AN 135:40152 CA
TI A polymeric microfluidic chip for CE/MS determination of small molecules
AU Kameoka, Jun; Craighead, Harold G.; Zhang, Hongwei; Henion, Jack
CS School of Applied and Engineering Physics, Cornell University, Ithaca, NY, 14853, USA
SO Analytical Chemistry (2001), 73(9), 1935-1941
AB A polymeric microfluidic chip made of Zeonor 1020 was fabricated using conventional embossing techniques to perform capillary electrophoresis for selected ion monitoring and selected reaction monitoring mass spectrometric detection of small mols. A silicon master was microfabricated using photolithog. and dry etching processes. The microfluidic channel was embossed in the plastic from a silicon master. The embossed chip was thermally bonded with a Zeonor 1020 cover to form an enclosed channel. This channel (60-μm width, 20-μm depth, 2.0- and 3.5-cm length) provided capillary electrophoresis (CE) sepn. of polar small mols. without surface treatment of the polymer. A microsprayer coupled via a microliquid junction provided

direct electrospray mass spectrometric detection of CE-sepd. components. An elec. field of 0.5-2 kV/cm applied between the microsprayer and a sepn. buffer reservoir produced a sepn. of carnitine, acetylcarnitine, and butyrylcarnitine with sepn. efficiencies ranging from 1650 to 18,000 plates. Injection quantities of 0.2 nmol of these compds. produced a sepn. of the targeted polar small mols. without surface treatment of the polymer-abundant ion current signals and baseline sepn. of these compds. in <10 s. These results suggest the feasibility of polymeric chip-based devices for ion spray CE/MS applications.

L12 ANSWER 46 OF 277 CA COPYRIGHT 2002 ACS
AN 135:4645 CA
TI Integrated Plastic Microfluidic Devices with ESI-MS for Drug Screening and Residue Analysis
AU Jiang, Yun; Wang, Pen-Cheng; Locascio, Laurie E.; Lee, Cheng S.
CS Department of Chemistry and Biochemistry, University of Maryland, College Park, MD, 20742, USA
SO Analytical Chemistry (2001), 73(9), 2048-2053
AB For this work, two different plastic microfluidic devices are designed and fabricated for applications in high-throughput residue anal. of food contaminants and drug screening of small-mol. libraries. Microfluidic networks on copolyester and poly(dimethylsiloxane) substrates are fabricated by silicon template imprinting and capillary molding techniques. The first device is developed to perform affinity capture, concn., and direct identification of targeted compds. using electrospray ionization mass spectrometry. Poly(vinylidene fluoride) membranes sandwiched between the imprinted copolyester microchannels in an integrated platform provide continuous affinity dialysis and concn. of a reaction mixt. contg. aflatoxin B1 antibody and aflatoxins. The second microfluidic device is composed of microchannels on the poly(dimethylsiloxane) substrates. The device is designed to perform miniaturized ultrafiltration of affinity complexes of phenobarbital antibody and barbiturates, including the sequential loading, washing, and dissocn. steps. These microfabricated devices not only significantly reduce dead vol. and sample consumption but also increase the detection sensitivity by at least 1-2 orders of magnitude over those reported previously. Improvements in detection sensitivity are attributed to analyte preconcn. during the affinity purifn. step, limited analyte diln. in the microdialysis junction, minimal sample loss, and the amenability of ESI-MS to nanoscale sample flow rates.

L12 ANSWER 49 OF 277 CA COPYRIGHT 2002 ACS
AN 134:363466 CA
TI Integrated microfluidic system enabling protein digestion, peptide separation, and protein identification
AU Gao, Jun; Xu, Jingdong; Locascio, Laurie E.; Lee, Cheng S.
CS Department of Chemistry and Biochemistry, University of Maryland, College Park, MD, 20742, USA
SO Analytical Chemistry (2001), 73(11), 2648-2655
AB An integrated platform is presented for rapid and sensitive protein identification by online protein digestion and anal. of digested proteins using electrospray ionization mass spectrometry or transient capillary isotachophoresis/capillary zone electrophoresis with mass spectrometry detection. A miniaturized membrane reactor is constructed by fabricating the microfluidic channels on a poly(dimethylsiloxane) substrate and coupling the microfluidics to a poly(vinylidene fluoride) porous membrane with the adsorbed trypsin. On the basis of he large surface area-to-vol. ratio of porous membrane media, adsorbed trypsin onto the poly(vinylidene fluoride) membrane is employed for achieving ultrahigh catalytic turnover. The

extent of protein digestion in a miniaturized membrane reactor can be directly controlled by the residence time of protein analytes inside the trypsin-adsorbed membrane, the reaction temp., and the protein concn. The resulting peptide mixts. can either be directly analyzed using electrospray ionization mass spectrometry or further concd. and resolved by electrophoretic sepns. prior to the mass spectrometric anal. This microfluidic system enables rapid identification of proteins in minutes instead of hours, consumes very little sample (nanogram or less), and provides online interface with upstream protein sepn. schemes for the anal. of complex protein mixts. such as cell lysates.

L12 ANSWER 55 OF 277 CA COPYRIGHT 2002 ACS
AN 134:348937 CA
TI High throughput DNA sequencing by direct monitoring of incorporation of fluorescent base analogs using a microfluidic device
IN Quake, Stephen; Volkmuth, Wayne; Unger, Marc
PA California Institute of Technology, USA
SO PCT Int. Appl., 73 pp.
PI WO 2001032930 A1 20010510 WO 2000-US30591 20001106
US 2001054778 A1 20011227 US 2001-796378 20010228
PRAI US 1999-163742P P 19991104
AB Methods for high speed, high throughput anal. of polynucleotide sequences, and apparatuses with which to carry out the methods are provided in the invention. The method is based on primer extension in a microfluidic device. Incorporation of dye-labeled base analogs into the primer is measured directly, eliminating the need to fractionate the primer extension products.

L12 ANSWER 56 OF 277 CA COPYRIGHT 2002 ACS
AN 134:341186 CA
TI Polymer microfluidics: the technology chain
AU Becker, Holger; Roetting, Oliver; Roepke, Wilfried; Heim, Ulf
CS Jenoptik Mikrotechnik GmbH, Jena, D-07745, Germany
SO Proceedings of SPIE-The International Society for Optical Engineering (2000), 4177(Microfluidic Devices and Systems III), 106-111
AB A review with 15 refs. In addn. to existing microfabrication technologies for the manufg. of glass or silicon-based microfluidic devices, the increasing demand for polymer based systems requires the establishment of equiv. technologies for the microstructuring of polymers. These technologies can be divided into two fields, the structuring of the polymer itself and the subsequent back-end processes. This article describes a complete technol. chain covering these two technol. fields.

L12 ANSWER 58 OF 277 CA COPYRIGHT 2002 ACS
AN 134:328347 CA
TI Miniaturized fluid transfer device
IN Wachs, Timothy; Henion, Jack D.
PA Cornell Research Foundation, Inc., USA
SO PCT Int. Appl., 37 pp.
PI WO 2001032245 A1 20010510 WO 2000-US28875 20001102
PRAI US 1999-163264P P 19991103
AB A miniaturized ion sprayer device is suitable for coupling with chip-based anal. sepn. devices, multi-well plates, or surfaces contg. residues of prepd. samples. One embodiment is a micro sprayer device, which is suitable for coupling to the terminal edge of a capillary electrophoresis (CE) chip, is constructed from a modified HPLC tubing and assocd. fittings and employs a free-standing liq. junction formed via continuous delivery of a flow (1-6 μL/min) of suitable solvent, which carries effluent through a pneumatically-assisted electrospray (ion spray) needle.

L12 ANSWER 59 OF 277 CA COPYRIGHT 2002 ACS
AN 134:322925 CA
TI Microfabricated PDMS multichannel emitter for electrospray ionization mass spectrometry
AU Kim, J.-S.; Knapp, D. R.
CS Department of Pharmacology, Medical University of South Carolina, Charleston, SC, USA
SO Journal of the American Society for Mass Spectrometry (2001), 12(4), 463-469
AB A novel microfabricated multichannel emitter for electrospray ionization mass spectrometry (ESI-MS) was implemented with polydimethylsiloxane (PDMS) using a soft lithog. technique. The emitters are formed as electrospray tips along a thin membrane on the edge of the device with channels of 100 μm × 30 μm dimensions. The electrospray performance of the PDMS emitters for a single channel device and a four channel device interfaced with a time-of-flight mass spectrometer was evaluated for detecting the mol. wt. of ref. peptides (angiotensin I and bradykinin). The emitters were durable at the flow rate of 1-20 μL min-1 for more than 30 h of continuous electrospray with limit of detection of 1 μM (S/N 18). This microfabrication method for a PDMS multichannel emitter as an integral part of a microfluidic device will facilitate development of more complex microfluidic anal. systems using ESI-MS.

L12 ANSWER 60 OF 277 CA COPYRIGHT 2002 ACS
AN 134:307464 CA
TI On-chip proteolytic digestion and analysis using "Wrong-Way-Round" electrospray time-of-flight mass spectrometry
AU Lazar, Iulia M.; Ramsey, Roswitha S.; Ramsey, J. Michael
CS Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, 37831-6365, USA
SO Analytical Chemistry (2001), 73(8), 1733-1739
AB Rapid protein digestion and anal. using a hybrid microchip nanoelectrospray device and time-of-flight mass spectrometry detection are reported. The device consists of a planar glass chip with microfabricated channels coupled to a disposable nanospray emitter. Reactions between substrate and enzyme (trypsin), mixed off-chip and then immediately loaded into a sample reservoir on the device, are monitored in real time following the onset of electrospray. Protein cleavage products are detd. at the optimum pH for generating tryptic fragments, directly from the digestion buffer using "wrong-way-round" electrospray, i.e., monitoring (MH)+ ions from basic solns. Intense tryptic peptide ions are obsd. within a few minutes following sample loading on the microchip. Proteins were identified from low femtomole or even attomole quantities of analyte/spectrum using peptide mass fingerprinting, loading 0.1-2 pmol/μL of sample on the chip. The sequence coverage for analyzed proteins ranged from 70 to 95%. The rapid anal. of human Hb is demonstrated using the technique.

L12 ANSWER 62 OF 277 CA COPYRIGHT 2002 ACS
AN 134:289162 CA
TI Modular microfluidic devices comprising layered circuit board-type substrates
IN O'Connor, Stephen D.; Dantsker, Eugene
PA Nanostream, Inc., USA
SO PCT Int. Appl., 53 pp.
PI WO 2001025137 A1 20010412 WO 2000-US27313 20001004
PRAI US 1999-157565P P 19991004
AB The present invention provides modular microfluidic devices and systems, as

well as methods for their manuf. A microfluidic device comprises a 1st substrate (30) having on at least a 1st surface thereof at least one microstructure (35) adapted to support a fluid, the microstructure being bounded by metallic features (34), such that the metallic features and the 1st surface together define inner walls of the microstructure. In addn., the device includes a 2nd substrate (39) sealed to the 1st substrate to define the microstructure there between, the 2nd substrate defining another inner wall of the microstructure, wherein the sealing is provided by an intermediate sealant coat (38) applied to at least a portion of at least one of the 1st substrate and the 2nd substrate. Preferably, the 1st substrate was prepd. by etching a circuit board comprising a metal (e.g., Cu) laminate (31). These microfluidic device can be rapidly prototyped with low tool-up cost, and can be easily assembled to form three-dimensional structures having complex microfluidic system geometries.

L12 ANSWER 63 OF 277 CA COPYRIGHT 2002 ACS
AN 134:277473 CA
TI Sequential Electrospray Analysis Using Sharp-Tip Channels Fabricated on a Plastic Chip
AU Yuan, Cheng-Hui; Shiea, Jentaie
CS Department of Chemistry, National Sun Yat-Sen University, Kaohsiung, Taiwan
SO Analytical Chemistry (2001), 73(6), 1080-1083
AB A disposable plastic (poly(Me methacrylate)) chip contg. eight open channels (375 μm in width, 300 μm in depth, 1.25 cm in length) capable of performing sequential electrospray anal. was described. The channels were constructed by simply cutting the plastic chip with a sharp knife. One end of each channel was fabricated to a sharp end, while the other was connected to a sample well. The high voltage required for electrospray was introduced into the sample soln. (70% methanol/water) via a copper electrode inserted in the sample well. The soln. in the sample well was continuously drawn to the sharp end of the channel by capillary action and by applying the electrospray voltage at the sample reservoir. A stable and fine Taylor cone was obsd. at the exit of the channel. Chem. modification on the surface of the channel was not required to decrease wettability. The octagonal plastic chip allowed sequential electrospray analyses of eight samples. The technique was also shown to be useful in rapidly detg. active ingredient in a com. tablet.

L12 ANSWER 67 OF 277 CA COPYRIGHT 2002 ACS
AN 134:208810 CA
TI Polymer microfluidic valves, membranes and coatings
AU Jo, Byung-Ho; Moorthy, Jaisree; Beebe, David J.
CS kman Institute for Advanced Science and Technology, University of Illinois, Urbana-Champaign, IL, 61801, USA
SO Micro Total Analysis Systems 2000, Proceedings of the μTAS Symposium, 4th, Enschede, Netherlands, May 14-18, 2000 (2000), 335-338. Editor(s): Van den Berg, Albert; Olthuis, W.; Bergveld, Piet. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
AB We present work in two areas of practical importance in polymer-based microfluidic systems, normally closed valves and redn. of swelling in org. solvents. A normally closed valve was designed, fabricated and characterized. The valve consists of three laminated layers [two polydimethylsiloxane (PDMS) micro-molded layers and a microscope cover glass]. A flexible membrane (diaphragm) creates a tight seal against a channel/dam structure. If sufficient driving pressure is present in the fluid channel, the membrane diaphragm is pushed upward allowing flow. The pressures required to open a variety of valves designs were measured. The hold off pressure of the valve can be controlled by adjusting the pressure that is applied

externally to the top of diaphragm. No leaking in the off state was obsd. Another issue in polymer microfluidic systems is polymer swelling in org. solvents. To make the inner walls of the devices hydrophilic and resistant to org. solvents, a flow through process is used to create a thin silicate barrier layer. The swelling of a square pattern in toluene was tested for different no. of coatings. The coating decreased the swelling by a factor of 2.

L12 ANSWER 71 OF 277 CA COPYRIGHT 2002 ACS
AN 134:183923 CA
TI Three-dimensional silicone device fabrication and inter-connection scheme for microfluidic applications using sacrificial wax layers
AU Dharmatilleke, Saman; Henderson, H. Thurman
CS Center for Microelectronic Sensors and MEMS Department of Electrical Computer Engineering and Computer Science, University of Cincinnati, Cincinnati, OH, 45221, USA
SO Micro-Electro-Mechanical Systems (2000), 2, 413-418
AB A simple room-temp. procedure is reported herein for formation of true three-dimensionality of microfluidic components and complete microfluidic systems in silicone elastomer, this is achieved by molding the plastic to simply encapsulate a pre-formed network of sacrificial wax threads or other connected wax configurations which are ultimately to become micro channels, microfluidic components and cavities in the plastic motherboard. When these wax sacrificial areas are etched away with acetone, precise cavities, channels, and capillaries result with direct arbitrary three-dimensionality. This method leads also to a simple and effective external interconnection scheme where ordinary fused SiO2 tubes may be press-fitted into the surface opening to withstand high pressure. An array of micro channels having circular cross sections with diams. of 100, 150 and 200 μm, membrane type valves, pinch valves, mixing chambers and reservoirs for fluid storage were molded in silicone elastomer using wax filaments. The wax filaments were dissolved in acetone after the silicone elastomer became hardened, leaving the micro channels, valves, mixing chambers and reservoirs in the silicone elastomer. This scheme gives the flexibility of allowing multi stacks of components (motherboards) while being able to control the channel lengths within the stacks as desired.

L12 ANSWER 77 OF 277 CA COPYRIGHT 2002 ACS
AN 134:159698 CA
TI Chip-based capillary electrophoresis/mass spectrometry determination of carnitines in human urine
AU eng, Yuzhong; Henion, Jack; Li, Jianjun; Thibault, Pierre; Wang, Can; Harrison, D. Jed
CS Analytical Toxicology, New York State College of Veterinary Medicine Cornell University, Ithaca, NY, 14850, USA
SO Analytical Chemistry (2001), 73(3), 639-646
AB chip-based capillary electrophoresis/mass spectrometry (CE/MS) system is described for the CE sepn. and online electrospray detection of carnitine and selected acylcarnitines from mixts. of anal. stds. as well as exts. of fortified human urine. Chip-based CE/MS expts. in two different labs. were carried out using a triple-quadrupole mass spectrometer and a quadrupole time-of-flight (QTOF) mass spectrometer, resp. The glass chips used with both systems were comparably equipped with a microfabricated capillary electrophoresis (CE) channel but with different electrosprayers. The quadrupole chip-based CE/MS expts. employed a miniature coupled microsprayer, which allowed coupling of the microelectrospray process via a micro liq. junction at the exit of the CE capillary channel. Selected ion monitoring (SIM) CE/MS expts. were employed for all of the quadrupole CE/MS work. The

QTOF CE/MS full-scan single MS and MS/MS expts. were carried out in another lab. using accurate mass measurement TOF mass spectrometry techniques. The electrospray process that was employed with the QTOF system differed in that an inserted nanoelectrospray capillary needle was carefully affixed into a flat-bottomed hole that was aligned with the CE channel exit orifice. SIM CE/MS using the described quadrupole system provided acceptable ion current electropherograms from fmole levels from anal. std. solns. of carnitine and acylcarnitines that were manually injected (loaded) onto the chip. In addn., the corresponding electropherograms for human urine fortified with the target carnitine and acylcarnitines at a 10-20 μg/mL (35-124 μM) level were obtained via SIM CE/MS techniques. The measured CE sepn. efficiency for the SIM CE/MS electropherograms was detd. to be 2860 plates (peak width at half-height method or N = 5.54(T/W0.52), and carnitine and three acylcarnitines were sepd. in less than 48 s. In contrast, using quadrupole-TOF technologies, the same samples could be dild. by a factor of 2-4 to obtain a comparable detector response for the target compds. In the full-scan, single mass analyzer mode (m/z 150-500), the CE sepn. efficiency was measured to be 2600 plates, but mass measurement accuracy was less than 5.0 ppm for the quaternary cations. In the CE/MS/MS mode, full-scan collision-induced dissocn. (CID) mass spectra were obtained with a mass accuracy of ≤10 ppm for the higher mass ions and ≤27 ppm for the lower mass product ions. These results demonstrate the feasibility for on-chip CE sepn. and electrospray mass spectrometric detection for these important compds. in synthetic mixts., as well as in human urine exts.

L12 ANSWER 78 OF 277 CA COPYRIGHT 2002 ACS
AN 134:159631 CA
TI Electrospray device for coupling microscale separations and other miniaturized devices with electrospray mass spectrometry
AU Wachs, Timothy; Henion, Jack
CS Analytical Toxicology Department of Population Medicine and Diagnostic Sciences, New York State College of Veterinary Medicine Cornell University, Ithaca, NY, 14850, USA
SO Analytical Chemistry (2001), 73(3), 632-638
AB A miniaturized ion sprayer device is described which is suitable for coupling with chip-based anal. sepn. devices, multiwell plates, or surfaces contg. residues of prepd. samples. Two versions of a similar device are described. A "microsprayer" device suitable for coupling to the terminal edge of a capillary electrophoresis (CE) chip is constructed from modified 1/16-in. HPLC fittings. This microsprayer employs a free-standing liq. junction formed via continuous delivery of a flow (2-6 μL/min) of suitable solvent which carries the CE effluent through a pneumatically assisted electrospray (ion spray) needle positioned in front of an atm. pressure ionization (API) mass spectrometer. A related but larger "minisprayer" device is also described which employs the same features as the microsprayer, but with an extended sampling capillary tube which can reach into the depths of 96-, 384-, and 1536-multiwell plates contg. either sample solns. or dried sample residues. The minisprayer may be positioned in front of an API ion sampling orifice and the multiwell plate positioned stepwise from sample to sample for anal. of trace samples contained in the wells. The resulting infusion-ion spray mass spectrometric analyses can provide sequential anal. of previously prepd. biol. samples contg. small drug compds., proteins, and related compds. This same device is also shown to be useful for sampling from a surface contg. trace level compds. of biol. interest. Results are shown that demonstrate microscale sepns. and selected ion monitoring (SIM) capillary electrophoresis/mass spectrometry (CE/MS) detection of berberine and palmatine using the microsprayer. SIM ion spray detn. of a 2 ng/μL soln. of berberine contained as a dry residue

in the bottom of a 384-well plate as well as full-scan electrospray mass spectra for low-picomole levels of cytochrome c contained in a 1536-well microtiter plate are shown. The resp. micro- and minisprayer devices provide a simple yet effective means of transferring trace-level samples either from a microscale or chip-based sepn. device as well as samples contained in multiwell plates which are increasingly employed in high-throughput applications in the pharmaceutical industry.

L12 ANSWER 79 OF 277 CA COPYRIGHT 2002 ACS
AN 134:159597 CA
TI Examination of dielectrophoretic behavior of DNA as a function of frequency from 30 Hz to 1 mhz using a flexible microfluidic test apparatus
AU Crippen, Shane M.; Holl, Mark R.; Meldrum, Deirdre R.
CS Department of Electrical Engineering, Genomation Laboratory, University of Washington, Seattle, WA, 98195-2500, USA
SO Micro Total Analysis Systems 2000, Proceedings of the μTAS Symposium, 4th, Enschede, Netherlands, May 14-18, 2000 (2000), 529-532. Editor(s): Van den Berg, Albert; Olthuis, W.; Bergveld, Piet. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
AB A microfluidic test app. for examg. dielectrophoretic (DEP) trapping as a method for purifn. and concn. of DNA from PCR and sequencing reaction products is presented. The device is comprised of a set of 4 independently addressable interdigitated gold microelectrode traps-microfluidic delivery of sample is performed using micro-molded poly(dimethylsiloxane) (PDMS) channels. The trapping behavior of fluorescently labeled DNA was obsd. under applied elec. fields at frequencies of 30 Hz, 100 Hz, 1 kHz, 10 kHz, 100 kHz, and 1 MHz and at applied voltages between 0.5 Vp-p and 20 Vp-p. Trapping behavior was obsd. to exhibit a strong frequency dependence suggesting that different modes of trapping are present in different excitation regions.

L12 ANSWER 80 OF 277 CA COPYRIGHT 2002 ACS
AN 134:159586 CA
TI Microchip-nano-electrospray device for rapid on-chip digestion and mass spectrometric analysis of hemoglobin variants
AU Lazar, Iulia M.; Ramsey, Roswitha S.; Ramsey, J. Michael
CS Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, 37831-6142, USA
SO Micro Total Analysis Systems 2000, Proceedings of the μTAS Symposium, 4th, Enschede, Netherlands, May 14-18, 2000 (2000), 379-382. Editor(s): Van den Berg, Albert; Olthuis, W.; Bergveld, Piet. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
AB The emerging technol. of microfabrication has generated devices that enable the completion of complex chem. processes on highly integrated miniaturized platforms. We have recently developed a microchip-nanoelectrospray device capable of providing subattomole sensitivity for peptide and protein samples [1]. A major advantage of this miniaturized electrospray platform is that it can operate as a stand-alone device, without any external assistance for stabilizing the electrospray. In this present manuscript we report on its applicability to the rapid anal. of on-chip generated proteolytic digestion fragments of Hb variants using time-of-flight mass spectrometric (TOFMS) detection. The amt. of initial protein consumed, sufficient for pos. identification using peptide mass fingerprinting, ranges in the low femtomole to attomole region.

L12 ANSWER 90 OF 277 CA COPYRIGHT 2002 ACS
AN 134:53251 CA
TI Microfluidic devices on polymer substrates for bioanalytical applications

AU Lin, Yuehe; Matson, Dean W.; Kurath, Dean E.; Wen, Jenny; Xiang, Fan; Bennett, Wendy D.; Martin, Peter M.; Smith, Richard D.
CS Pacific Northwest National Laboratory, Richland, WA, 99352, USA
SO Microreaction Technology: Industrial Prospects, Proceedings of the International Conference on Microreaction Technology, 3rd, Frankfurt, Apr. 18-21, 1999 (1999), 451-460. Editor(s): Ehrfeld, Wolfgang. Publisher: Springer-Verlag, Berlin, Germany.
AB The development of capabilities to miniaturize anal. devices and components offers a no. of potential benefits. Among these are the ability to reduce sample sizes, development of low cost, single-use disposable devices, and improved device portability. Extensive work has been done on producing such microanal. systems on silicon or glass substrates using processes commonly employed in electronic chip manufg. However, for many anal. applications, common polymeric materials provide acceptable substrates from which to produce components or complete anal. systems. The low flow rate characteristic of these microfluidic devices is compatible with the electrospray ionization/mass spectrometry. The development of microfluidic anal. devices fabricated on polymer substrates using excimer laser micro-machining technol. is described. These include a microfluidic motherboard, dual-stage microdialysis chip, and a micro-capillary isoelec. focusing device. The applications of these microdevices for cleanup, fractionation, and sepn. of biol. samples are discussed.

L12 ANSWER 95 OF 277 CA COPYRIGHT 2002 ACS
AN 133:358681 CA
TI Novel microfabricated device for electrokinetically induced pressure flow and electrospray ionization mass spectrometry
AU Lazar, Iulia M.; Ramsey, Roswitha S.; Jacobson, Stephen C.; Foote, Robert S.; Ramsey, J. Michael
CS Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, 37831-6365, USA
SO J. Chromatogr., A (2000), 892(1+2), 195-201
AB A novel microchip device for electrospray ionization was fabricated and interfaced to a time-of-flight mass spectrometer. Fluid is electrokinetically transported through the chip to a fine fused-silica capillary inserted directly into a channel at the edge of the device. Electrospray is established at the tip of the capillary, which assures a stable, efficient spray. The elec. potential necessary for electrospray generation and the voltage drop for electroosmotic pumping are supplied through an elec. permeable glass membrane contacting the fluidic channel holding the capillary. The membrane is fabricated on the microchip using std. photolithog. and wet chem. etching techniques. Performance relative to other microchip electrospray sources was evaluated and the device tested for potential use as a platform for online electrophoretic detection. Sensitivity is approx. three orders of magnitude better than spraying from the flat edge of the chip. The effect of the capillary on electroosmotic flow was examd. both exptl. and theor.

L12 ANSWER 99 OF 277 CA COPYRIGHT 2002 ACS
AN 133:307282 CA
TI System and method for high throughput mass spectrometric analysis
IN Karger, Barry L.; Felten, Chantal; Foret, Frantisek; Zhang, Bailin
PA Northeastern University, USA
SO PCT Int. Appl., 37 pp.
PI WO 2000062039 A1 20001019 WO 2000-US9480 20000410
PRAI US 1999-128509P P 19990409
AB Automated liq. handling infusion system are described which comprise a microscale sample holder configured for holding multiple samples and

situated in conjunction with a positioning system capable of automated operation; a sample infusion capillary having an inlet end which is aligned with one of the multiple samples in the sample holder; and a source of pos. or neg. pressure for applying the pos. or neg. pressure across the sample infusion capillary. Liq. handling reservoir systems are also described which comprise a microfluidic device comprising multiple microfabricated channels, each channel having an inlet end; a detachable reservoir manifold external to the device and having at least one opening for fluid flow into and out of the reservoir, the reservoir positioned so that the reservoir opening is proximate to an inlet end of a microfabricated channel in the device for fluid flow between the reservoir and the channel; and a source of pos. or neg. pressure for applying the pos. or neg. pressure across the system. The reservoirs of the manifold may be sepd. from the microfluidic device by a semipermeable membrane. The membrane may be used for electro-osmotic pumping of the liq. to or from the manifold to the microfluidic device or for sample preconcn., or it may contain an immobilized reagent for sample modification (e.g., an enzyme ot a reagent which forms a fluor-escent label on the mols. being analyzed). Application to high throughput mass spectrometric anal. (e.g., in pharmacokinetic studies) is indicated.

L12 ANSWER 101 OF 277 CA COPYRIGHT 2002 ACS
AN 133:301306 CA
TI Chip-based capillary electrophoresis with an electrodeless nanospray interface
AU Vrouwe, Elwin X.; Gysler, Jens; Tjaden, Ubbo R.; Van der Greef, Jan
CS Department of Analytical Chemistry, Leiden/Amsterdam Center for Drug Research, Leiden University, Leiden, 2300 RA, Neth.
SO Rapid Commun. Mass Spectrom. (2000), 14(18), 1682-1688
AB A sheathless and electrodeless nanospray interface was used to interface a polycarbonate capillary electrophoresis (CE) chip to a mass spectrometer (MS). The chip was made of two flat polycarbonate plates which were bolted together. Channels were imprinted in one of the plates with metal wires, using a hydraulic press. A short tapered capillary connected to the chip was used as the nanospray emitter. The advantage of this electrodeless interface is that it was not necessary to apply a electrospray voltage to the chip or the nanospray emitter. Instead, the CE voltage already applied to the buffer compartment on the chip, to drive the electrophoresis, was used to generate the spray also. A low cond. buffer of 1.25 mmol/L ammonium acetate in 80% methanol was used to obtain a large elec. field across the buffer channel. The performance of the device was evaluated by analyzing a mixt. of three β-agonists Relative std. deviation (RSD) values obtained were between 4.8 and 5.0%. A sample concn. of 40 nmol/L resulted in a signal-to-noise ratio of 2 to 5 for the different components. Compared to a conventional CE anal. in a fused silica capillary with UV detection, only a minor loss of resoln. was obsd., which can be attributed to the design of the chip.

L12 ANSWER 104 OF 277 CA COPYRIGHT 2002 ACS
AN 133:278116 CA
TI Integration of immobilized trypsin bead beds for protein digestion within a microfluidic chip incorporating capillary electrophoresis separations and an electrospray mass spectrometry interface
AU Wang, Can; Oleschuk, Richard; Ouchen, Fahima; Li, Jianjun; Thibault, Pierre; Harrison, D. Jed
CS Dept. of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2, Can.
SO Rapid Commun. Mass Spectrom. (2000), 14(15), 1377-1383
AB A microfluidic device is described in which an electrospray interface to a mass spectrometer is integrated with a capillary electrophoresis channel,

an injector and a protein digestion bed on a monolithic substrate. A large channel, 800 μm wide, 150 μm deep and 15 mm long, was created to act as a reactor bed for trypsin immobilized on 40-60 μm diam. beads. Sepn. was performed in channels etched 10 μm deep, 30 μm wide and about 45 mm long, feeding into a capillary, attached to the chip with a low dead vol. coupling, that was 30 mm in length, with a 50 μm i.d. and 180 μm o.d. Sample was pumped through the reactor bed at flow rates between 0.5 and 60 μL/min. The application of this device for rapid digestion, sepn. and identification of proteins is demonstrated for melittin, cytochrome c and bovine serum albumin (BSA). The rate and efficiency of digestion was related to the flow rate of the substrate soln. through the reactor bed. A flow rate of 1 or 0.5 μL/min was found adequate for complete consumption of cytochrome c or BSA, corresponding to a digestion time of 3-6 min at room temp. Coverage of the amino acid sequence ranged from 92% for cytochrome c to 71% for BSA, with some missed cleavages obsd. Melittin was consumed within 5 s. In contrast, a similar extent of digestion of melittin in a cuvet took 10-15 min. The kinetic limitations assocd. with the rapid digestion of low picomole levels of substrate were minimized using an integrated digestion bed with hydrodynamic flow to provide an increased ratio of trypsin to sample. This chip design thus provides a convenient platform for automated sample processing in proteomics applications.

L12 ANSWER 105 OF 277 CA COPYRIGHT 2002 ACS
AN 133:267383 CA
TI Polymer-based electrospray chips for mass spectrometry
AU Wang, Xuan-Qi; Desai, Amish; Tai, Yu-Chong; Licklider, Lawrence; Lee, Terry D.
CS California Institute of Technology, Pasadena, CA, 91125, USA
SO IEEE Int. Conf. Micro Electro Mech. Syst., Tech. Dig., 12th (1999), 523-528 Publisher: Institute of Electrical and Electronics Engineers, New York, N. Y.
AB In this paper, we present our development of a MEMS chip with an overhanging polymer microcapillary 2.5 mm in length and with a 5 μm × 10 μm orifice size at the tip. The fabricated chips have been successfully interfaced with a mass spectrometer (MS) to validate electrospray ionization (ESI) for biochem. anal. The prediction of a redn. in Taylor cone size has also been obsd. with real time ESI fluid visualization from our chip. Built-in micro particle filters and centimeter long serpentine micro channels were fabricated on the chip with a low temp. process by using the Parylene polymer as a structural material, aluminum and photoresist as sacrifical layers, and bromine triflouride (BrF3) gas phase etching for final microcapillary releasing. The use of an overhanging polymer structure adds a new a level of mech. robustness that was never achievable with other thin films. Functionality of our device was proven by consistent detection of Myoglobin in a 200 nM soln. at a flow rate of 35nL/min and a voltage potential of 1.5 kV. This MS interface chip represents vital and significant improvements in MEMS process technol. and MS functionality with respect to the silicon nitride (SixNy) ESI nozzles previously reported by our group.

L12 ANSWER 110 OF 277 CA COPYRIGHT 2002 ACS
AN 133:234554 CA
TI A Fully Integrated Monolithic Microchip Electrospray Device for Mass Spectrometry
AU Schultz, Gary A.; Corso, Thomas N.; Prosser, Simon J.; Zhang, Sheng
CS Advanced BioAnalytical Services Inc., Ithaca, NY, 14850, USA
SO Anal. Chem. (2000), 72(17), 4058-4063
AB A novel microfabricated nozzle has been developed for the electrospray of liqs. from microfluidic devices for anal. by mass spectrometry. The

electrospray device was fabricated from a monolithic silicon substrate using deep reactive ion etching and other std. semiconductor techniques to etch nozzles from the planar surface of a silicon wafer. A channel extends through the wafer from the tip of the nozzle to a reservoir etched into the opposite planar surface of the wafer. Nozzle diams. as small as 15 μm have been fabricated using this method. The microfabricated electrospray device provides a reproducible, controllable, and robust means of producing nano-electrospray of a liq. sample. The electrospray device was interfaced to an atm. pressure ionization time-of-flight mass spectrometer using continuous infusion of test compds. at low nanoliter-per-minute flow rates. Nozzle-to-nozzle signal intensity reproducibility using 10 nozzles was demonstrated to be 12% with single-nozzle signal stability routinely less than 4% relative std. deviation (RSD). Solvent compns. have been electrosprayed ranging from 100% org. to 100% aq. The signal-to-noise ratio from the infusion of a 10 nM cytochrome c soln. in 100% water at 100 nL/min was 450:1. Microchip electrospray nozzles were compared with pulled capillaries for overall sensitivity and signal stability for small and large mols. The microchip electrospray nozzles showed a 1.5-3-times increase in sensitivity compared with that from a pulled capillary, and signal stability with the microchip was 2-4% RSD compared with 4-10% with a pulled capillary. Electrospray device lifetimes achieved thus far have exceeded 8 h of continuous operation and should be sufficient for typical microfluidic applications. The total vol. of the electrospray device is less than 25 pL, making it suitable for combination with microfluidic sepn. devices.

L12 ANSWER 112 OF 277 CA COPYRIGHT 2002 ACS
AN 133:202427 CA
TI Integrated monolithic microfabricated dispensing nozzle and liquid chromatography-electrospray system and method
IN Schultz, Gary A.; Corso, Thomas N.
PA Advanced Bioanalytical Services, Inc., USA
SO PCT Int. Appl., 127 pp.
PI WO 2000052455 A1 20000908 WO 2000-US5123 20000229
PRAI US 1999-122972P P 19990302
AB A droplet/electrospray device and a liq. chromatog.-electrospray system are disclosed. The droplet/ electrospray device comprises a substrate defining a channel between an entrance orifice on an injection surface and an exit orifice on an ejection surface, a nozzle defined by a portion recessed from the ejection surface surrounding the exit orifice, and an electrode for application of an elec. potential to the substrate to optimize and generate droplets or an electrospray. A plurality of these electrospray devices can be used as an array of miniaturized nozzles. The liq. chromatog.-electrospray device comprises a sepn. substrate defining an introduction channel between an entrance orifice and a reservoir and a sepn. channel between the reservoir and an exit orifice, the sepn. channel being populated with sepn. posts perpendicular to the fluid flow.

L12 ANSWER 113 OF 277 CA COPYRIGHT 2002 ACS
AN 133:195174 CA
TI Material transport method and apparatus for microchips
IN Ramsey, J. Michael; Ramsey, Roswitha S.
PA Lockheed Martin Energy Research Corporation, USA
SO U.S., 19 pp.
PI US 6110343 A 20000829 US 1996-726355 19961004
US 6231737 B1 20010515 US 1999-440892 19991116
PRAI US 1996-726355 A3 19961004
AB An electrospraying app. is described that uses a microchannel formed in a microchip. Fluid is pumped through the channel to an outlet orifice using

either hydraulic or electrokinetic means. An electrospray is generated by establishing a p.d. between the fluid at the outlet orifice and a target electrode spaced from the outlet orifice. Electrokinetic pumping is also utilized to provide addnl. benefits to microchip devices. Materials contg., e.g., peptides, proteins, DNA or synthetic polymers, that have been processed on the microchips can be transported by electrospraying to downstream analyzers, e.g., mass spectrometers.

L12 ANSWER 118 OF 277 CA COPYRIGHT 2002 ACS
AN 133:161399 CA
TI Development of Multichannel Devices with an Array of Electrospray Tips for High-Throughput Mass Spectrometry
AU Liu, Hanghui; Felten, Chantal; Xue, Quifeng; Zhang, Bailin; Jedrzejewski, Paul; Karger, Barry L.; Foret, Frantisek
CS Barnett Institute and Department of Chemistry, Northeastern University, Boston, MA, 02115, USA
SO Anal. Chem. (2000), 72(14), 3303-3310
AB The basic principles of multichannel devices with an array of electrospray tips for high-throughput infusion electrospray ionization mass spectrometry (ESI-MS) have been developed. The prototype plastic devices were fabricated by casting from a solvent-resistant resin. The sample wells on the device were arranged in the format of the std. 96-microtiter well plate, with each sample well connected to an independent electrospray exit port via a microchannel with imbedded electrode. A second plastic plate with distribution microchannels was employed as a cover plate and pressure distributor. Nitrogen gas was used to pressurize individual wells for transport of sample into the electrospray exit port. The design of independent microchannels and electrospray exit ports allowed very high throughput and duty cycle, as well as elimination of any potential sample carryover. The device was placed on a computer-controlled translation stage for precise positioning of the electrospray exit ports in front of the mass spectrometer sampling orifice. High-throughput ESI-MS was demonstrated by analyzing 96 peptide samples in 480 s, corresponding to a potential throughput of 720 samples/h. As a model application, the device was used for the MS detn. of inhibition consts. of several inhibitors of HIV-1 protease.

L12 ANSWER 120 OF 277 CA COPYRIGHT 2002 ACS
AN 133:147120 CA
TI Injection-molded, polymeric microfluidic devices coupled to electrospray ionization tandem mass spectrometers for protein identification
AU Figeys, Daniel; Aebersold, Ruedi; Lock, Chris
CS National Research Council of Canada, Halifax, NS, Can.
SO J. Capillary Electrophor. Microchip Technol. (1999), 6(1 & 2), 1-6
AB An injection-molded polymeric microfluidic device was coupled to two different types of electrospray ionization (ESI) mass spectrometers for protein identification. We demonstrate that tryptic digests of different proteins that were simultaneously present on the polymeric device could be successively mobilized with limited sample-to-sample cross-contamination toward an MS and identified by the collision-induced dissocn. (CID) spectra generated from selected peptides.

L12 ANSWER 123 OF 277 CA COPYRIGHT 2002 ACS
AN 133:116849 CA
TI Analytical microdevices for mass spectrometry
AU Oleschuk, R. D.; Harrison, D. J.
CS Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2, Can.
SO TrAC, Trends Anal. Chem. (2000), 19(6), 379-388

AB A review with 43 refs. The seemingly unlikely marriage between large mass spectrometers and small microchips is actually a good one. Microfluidic devices have been coupled to mass spectrometers using electrospray ionization interfaces. Different interface designs and various integrated protein prepn. and preconcn. procedures are reviewed. The potential role of chip-mass spectrometry in proteomics and drug discovery is also discussed.

L12 ANSWER 125 OF 277 CA COPYRIGHT 2002 ACS
AN 133:97441 CA
TI Re-configurable fluid circuits by PDMS elastomer micromachining
AU Armani, Deniz; Liu, Chang; Aluru, Narayan
CS Microelectronics Laboratory, University of Illinois, Urbana-Champaign, IL, 61801, USA
SO IEEE Int. Conf. Micro Electro Mech. Syst., Tech. Dig., 12th (1999), 222-227
Publisher: Institute of Electrical and Electronics Engineers, New York, N. Y.
AB The authors report on a microfabrication techniques for realizing re-configurable micro fluidics devices using polymethylsiloxane material (PDMS). The mech. characteristics of the material, including the Young's modulus and the adhesion energy were detd. exptl. The magnitude of Young's modulus ranges from 8.7 × 105 Pa to 3.6 × 105 Pa. The adhesion energy is a function of the PDMS compn. as well as chem. treatment. A method for efficiently developing flow interconnects was demonstrated.

L12 ANSWER 129 OF 277 CA COPYRIGHT 2002 ACS
AN 132:340961 CA
TI Polymer-based MEMS electrospray nozzle for mass spectrometry
IN Tai, Yu-Chong; Wang, Xuan-Qi; Desai, Amish; Lee, Terry D.; Licklider, Lawrence
PA California Institute of Technology, USA
SO PCT Int. Appl., 27 pp.
PI WO 2000030167 A1 20000525 WO 1999-US27500 19991118
PRAI US 1998-109264P P 19981119
AB A MEMS device with an overhanging polymer capillary (20) provides vital and significant improvements in interfacing a MEMS electrospray nozzle (50) to an MS inlet or other macroscopic instrumentation. The fabrication methodol. assocd. therewith is easily expanded to include built-in micro particle filters (71) and centimeter long serpentine micro channels (75) provided on-chip (19) and fabricated using a low temp. process.

L12 ANSWER 132 OF 277 CA COPYRIGHT 2002 ACS
AN 132:309249 CA
TI Polymers: an excellent and increasingly used material for microsystems
AU Bley, Peter
CS Microsystems Technol. Program, Forschungszentrum Karlsruhe, Karlsruhe, Germany
SO Proc. SPIE-Int. Soc. Opt. Eng. (1999), 3876(Micromachined Devices and Components V), 172-184
AB A review with 45 refs. Microsystems, whose main components are made of polymers, have meanwhile found a firm place in microsystems technol., both as important niche products and as bulk commodities. A large no. of structuring techniques are available, on the one hand, for primary structuring (electron beam, UV and X-ray lithog., laser patterning, stereo lithog., etc.) and, on the other hand, as replication techniques for low-cost mass prodn. (reactive injection molding, thermoplastic injection molding, hot embossing techniques, etc.). Microstructures made of polymers may be clearly cheaper to manuf. than those made of any other material. Besides polymers structured on a micrometer scale, also membranes made of

polymers are becoming increasingly more important in microsystems technol. The development of microstructure technol. with the use of polymers began at what is now Forschungszentrum Karlsruhe (Karlsruhe Research Center) in the early eighties. The development of both, deep X-ray lithog. and various molding techniques (LIGA) process started back then already. The large variety of possible uses will be shown by examples of developments originating from Forschungszentrum Karlsruhe. These mainly comprise microoptics (lenses, distance sensors, spectrometers, micro-optical benches, etc.), microfluidics (capillaries for 'labs on chip,' polymer membranes as basis for pumps, valves, pressure sensors, flow sensors, and sepg. systems), and actuators based on selectively inflatable chambers. Another example for the possible application of polymers in microsystems is their use as functional coating for electrochem. transducers (e.g. surface acoustic wave (SAW) sensors).

L12 ANSWER 133 OF 277 CA COPYRIGHT 2002 ACS
AN 132:273585 CA
TI Microfluidic devices connected to capillaries with minimal dead volume
IN Tang, Thompson; Harrison, D. Jed; Bings, Nicolas; Wang, Can; Ocvirk, Gregor; Li, Jianjun; Skinner, Cameron; Thibault, Pierre
PA University of Alberta, Can.; Institute for Biological Sciences
SO PCT Int. Appl., 41 pp.
PI WO 2000022409 A2 20000420 WO 1999-CA868 19990923
PRAI US 1998-169146 A1 19981009
AB A method is provided for joining a microchip device to a capillary tube. The microchip device has a capillary channel opening onto an edge surface of the device. A short hole is drilled into the edge surface, aligned with the capillary channel. The drilling is done with a flat bottom, preferably by a two-step drilling process. Then, the end of the capillary can be inserted into the hole so that its end is substantially flush with the flat bottom of the hole, thereby eliminating dead vol. Testing showed that this connection provides very little band broadening of samples transported through the capillary channel into the capillary tube. The tip of the capillary tube can be tapered, so that it is suitable for use as an electrospray source for a mass spectrometer.

L12 ANSWER 135 OF 277 CA COPYRIGHT 2002 ACS
AN 132:266011 CA
TI Fabrication of three-dimensional microfluidic systems by stacking molded polydimethylsiloxane (PDMS) layers
AU Jo, Byung-Ho; Beebe, David J.
CS Dep. Electr. and Computer Eng., Beckman Institute for Advanced Science and Technol., Univ. of Illinois, Urbana-Champaign, IL, USA
SO Proc. SPIE-Int. Soc. Opt. Eng. (1999), 3877(Microfluidic Devices and Systems II), 222-229
AB A new technique to fabricate 3D microchannels using polydimethylsiloxane (PDMS) elastomer material is presented. The process allows for the stacking of many thin (about 100 μm thick) patterned PDMS layers to realize complex 3D channel paths. Replica molding method is utilized to generate each layer. The master for each layer is formed on a silicon wafer using SU-8 pos. relief photoresist. PDMS is cast against the master producing molded layers contg. channels and openings. To realize thin layers with openings, a sandwich molding configuration was developed that allows precise control of the PDMS thickness. The master wafer is clamped within a sandwich that includes flat aluminum plates, a flexible polyester film layer, a rigid Pyrex wafer and a rubber sheet. A parametric study is performed on PDMS surface activation in a reactive ion etching (RIE) system and the subsequent methanol treatment for bonding and aligning very thin

individual components to a substrate. Low RF power and short treatment times are better than high RF power and long treatment times resp. for instant bonding. Layer to layer alignment of less than 15 μm is achieved with manual alignment techniques that utilize surface tension driven self alignment methods. A coring procedure is used to realize off chip fluidic connections via the bottom PDMS layer, allowing the top layer to remain smooth and flat for complete optical access. After fabricating 3D channel paths, the hydrophobic surfaces of the inside channel walls can be activated (hydrophobic to hydrophilic) an oxygen plasma RIE system.

L12 ANSWER 136 OF 277 CA COPYRIGHT 2002 ACS
AN 132:266010 CA
TI Fabrication of polymer high-aspect-ratio structures with hot embossing for microfluidic applications
AU Becker, Holger; Heim, Ulf; Roetting, O.
CS Jenoptik Mikrotechnik GmbH, Jena, Germany
SO Proc. SPIE-Int. Soc. Opt. Eng. (1999), 3877(Microfluidic Devices and Systems II), 74-79
AB In this paper we present the fabrication technologies necessary for the high vol. prodn. of microfluidic devices, with specific emphasis on the hot embossing process and the parameters necessary for achieving high aspect ratio structures on substrate like poly(Me methacrylate) or polycarbonate. In addn. to the replication technol., we have investigated subsequent process steps like via hole drilling, bonding and dicing. Several examples for different microfluidic applications are given.

L12 ANSWER 137 OF 277 CA COPYRIGHT 2002 ACS
AN 132:265980 CA
TI Characterizing the process of cast molding microfluidic systems
AU Chiang, Yuh-Min; Bachman, Mark; Chu, Charles Y.; Li, GuannPyng
CS Dep. Electr. and Computer Eng., Univ. of California at Irvine, Irvine, CA, USA
SO Proc. SPIE-Int. Soc. Opt. Eng. (1999), 3877(Microfluidic Devices and Systems II), 303-311
AB Cast molding is a simple, low cost microfabrication method which offers the potential to fabricate microstructures in a large variety of polymer materials. A cast molding technique is discussed which exploits the use of poly(di-Me siloxane) as a mold material. The suitability of this process for microfluidic systems with various polymers was studied by observing the mold sticking properties, pattern transfer resoln., and effects on surface roughness and surface wettability. The process yielded excellent results for all polymers, suggesting the suitability of cast molding as a general purpose microfabrication technique. The surface wettability was modified for some polymers.

L12 ANSWER 138 OF 277 CA COPYRIGHT 2002 ACS
AN 132:248079 CA
TI Laser micromachined isoelectric focusing devices on polymer substrate for electrospray mass spectrometry
AU Lin, Yuehe; Wen, Jenny; Fan, Xiang; Matson, Dean W.; Smith, Richard D.
CS Pacific Northwest National Lab., Richland, WA, USA
SO Proc. SPIE-Int. Soc. Opt. Eng. (1999), 3877(Microfluidic Devices and Systems II), 28-35
AB A microfabricated device for isoelec. focusing (IEF) incorporating an optimized electrospray ionization (ESI) tip was constructed on polycarbonate plates using a laser micromachining technique. The sepn. channels on an IEF chip were 16 cm long, 50 μm wide and 30 μm deep. Elec. potentials used for IEF focusing and electrospray were applied through platinum

electrodes placed in the buffer reservoirs, and which were isolated from the sepn. channel by mol. porous membranes. Online ESI produced directly from a sharp "tip" on the microchip was evaluated. The results indicate that this design can produce a stable electrospray that is further improved and made more flexible with the assistance of sheath gas and sheath liq. Error anal. of the spectral data shows that the std. deviation in signal intensity for an analyte peak was less than approx. 5% over 3 h. The prodn. of stable electrosprays directly from microchip IEF devices represents a step towards easily-fabricated microanal. devices. IEF sepns. of protein mixts. were demonstrated for uncoated polycarbonate microchips. Online IEF/ESI-MS was demonstrated using the microfabricated chip with an ion-trap ESI mass spectrometer for characterization of protein mixts.

L12 ANSWER 143 OF 277 CA COPYRIGHT 2002 ACS
AN 132:204962 CA
TI An enhanced microfluidic chip coupled to an electrospray Qstar mass spectrometer for protein identification
AU Pinto, Devanand M.; Ning, Yuebin; Figeys, Daniel
CS National Research Council-Canada, Halifax, NS, B3H 3Z1, Can.
SO Electrophoresis (2000), 21(1), 181-190
AB The combination of microfabricated fluidic systems (μFAB) and electrospray mass spectrometers (ESI-MS) will provide multiplexed and integrated anal. systems for proteins and other biomols. Implementation of this novel approach requires the development of robust and user-friendly μFAB devices. Here, we present new approaches that improve the robustness, user friendliness and performance of μFAB devices coupled to MS. First, we present the development of a convenient mount to connect a μFAB device to the ESI-MS and the incorporation of filters in the reservoirs and exit of the μFAB. This mount facilitates interfacing and significantly reduces the chem. noise obsd. by the MS. Furthermore, we demonstrate improvements in sample handling and delivery by using either a nonaq. electrolyte or a cationic coating on the surfaces in the μFAB device and transfer capillary. These improvements are applied to protein anal. by continuous infusion of proteolytic digests.

L12 ANSWER 144 OF 277 CA COPYRIGHT 2002 ACS
AN 132:191277 CA
TI Polymer microfabrication methods for microfluidic analytical applications
AU Becker, Holger; Gartner, Claudia
CS Jenoptik Mikrotechnik, Jena, D-07745, Germany
SO Electrophoresis (2000), 21(1), 12-26
AB A review with 64 refs. A growing no. of microsystem technol. (MST) applications, particularly in the field of microfluidics with its applications in the life sciences, have a need for novel fabrication methods which account for substrates other than silicon or glass. We present in this paper an overview of existing polymer microfabrication technologies for microfluidic applications, namely replication methods such as hot embossing, injection molding and casting, and the technologies necessary to fabricate the molding masters. In addn., techniques such as laser ablation and layering techniques are examd. Methods for bonding and dicing of polymer materials, which are necessary for complete systems, are evaluated.

L12 ANSWER 145 OF 277 CA COPYRIGHT 2002 ACS
AN 132:177688 CA
TI Separation and Identification of Peptides from Gel-Isolated Membrane Proteins Using a Microfabricated Device for Combined Capillary Electrophoresis/Nanoelectrospray Mass Spectrometry
AU Li, Jianjun; Kelly, John F.; Chernushevich, Igor; Harrison, D. Jed;

Thibault, Pierre
CS Institute for Biological Sciences, Ottawa, ON, K1A 0R6, Can.
SO Anal. Chem. (2000), 72(3), 599-609
AB The coupling of microfabricated devices to nanoelectrospray mass spectrometers using both a triple quadrupole and a quadrupole time-of-flight mass spectrometer (QqTOF MS) is presented for the anal. of trace-level membrane proteins. Short disposable nanoelectrospray emitters were directly coupled to the chip device via a low dead vol. connection. The anal. performance of this integrated device in terms of sensitivity and reproducibility was evaluated for std. peptide mixts. A concn. detection limit ranging from 3.2 to 43.5 nM for different peptides was achieved in selected ion monitoring, thus representing a 10-fold improvement in sensitivity compared to that of microelectrospray using the same chip/mass spectrometer. Replicate injections indicated that reproducibility of migration time was typically less than 3.1% RSD whereas RSD values of 6-13% were obsd. on peak areas. Although complete resoln. of individual components is not typically achieved for complex digests, the present chip capillary electrophoresis (chip-CE) device enabled proper sample cleanup and partial sepn. of multicomponent samples prior to mass spectral identification. Analyses of protein digests were typically achieved in less than 1.5 min with peak widths of 1.8-2.5 s (half-height definition) as indicated from individual reconstructed ion electropherograms. The application of this chip-CE/QqTOF MS system is further demonstrated for the identification of membrane proteins which form a subset of the Haemophilus influenzae proteome. Bands first sepd. by 1D-gel electrophoresis were excised and digested, and extd. tryptic peptides were loaded on the chip without any further sample cleanup or online adsorption preconcn. Accurate mol. mass detn. (<5 ppm) in peptide-mapping expts. was obtained by introducing an internal std. via a postsepn. channel. The anal. potential of this integrated device for the identification of trace-level proteins from different strains of H. influenzae is demonstrated using both peptide mass-fingerprint database searching and online tandem mass spectrometry.

L12 ANSWER 146 OF 277 CA COPYRIGHT 2002 ACS
AN 132:177606 CA
TI A microdevice with integrated liquid junction for facile peptide and protein analysis by capillary electrophoresis/electrospray mass spectrometry
AU Zhang, Bailin; Foret, Frantisek; Karger, Barry L.
CS Barnett Institute and Department of Chemistry, Northeastern University, Boston, MA, 02115, USA
SO Anal. Chem. (2000), 72(5), 1015-1022
AB A novel microfabricated device was implemented for facile coupling of capillary electrophoresis with mass spectrometry (CE/MS). The device was constructed from glass wafers using std. photolithog./wet chem. etching methods. The design integrated (a) sample inlet ports, (b) the sepn. channel, (c) a liq. junction, and (d) a guiding channel for the insertion of the electrospray capillary, which was enclosed in a miniaturized subatmospheric electrospray chamber of an ion trap MS. The replaceable electrospray capillary was precisely aligned with the exit of the sepn. channel by a microfabricated guiding channel. No glue was necessary to seal the electrospray capillary. This design allowed simple and fast replacement of either the microdevice or the electrospray capillary. The performance of the device was tested for CE/MS of peptides, proteins, and protein tryptic digests. Online tandem mass spectrometry was used for the structure identification of the protein digest products. High-efficiency/high-resoln. sepns. could be obtained on a longer channel (11 cm on-chip) microdevice, and fast sepns. (under 50 s) were achieved with a short (4.5

cm on-chip) sepn. channel. In the expts., both electrokinetic and pressure injections were used. The sepn. efficiency was comparable to that obtained from conventional capillary electrophoresis.

L12 ANSWER 147 OF 277 CA COPYRIGHT 2002 ACS
AN 132:143952 CA
TI Microfabricated isoelectric focusing device for direct electrospray ionization-mass spectrometry
AU Wen, Jenny; Lin, Yuehe; Xiang, Fan; Matson, Dean W.; Udseth, Harold R.; Smith, Richard D.
CS Environmental Molecular Science Laboratory, Pacific Northwest National Laboratory, Richland, WA, 99352, USA
SO Electrophoresis (2000), 21(1), 191-197
AB A novel microfabricated device for isoelec. focusing (IEF) incorporating an optimized electrospray ionization (ESI) tip was constructed on polycarbonate plates using laser micromachining. The IEF microchip incorporated a sepn. channel (50 μ × 30 μ × 16 cm), three fluid connectors, and two buffer reservoirs. Elec. potentials used for IEF focusing and electrospray were applied through platinum electrodes placed in the buffer reservoirs, which were isolated from the sepn. channel by porous membranes. Direct ESI-mass spectrometry (MS) using electrosprays produced directly from a sharp emitter "tip" on the microchip was evaluated. The results indicated that this design can produce a stable electrospray and that performance was further improved and made more flexible with the assistance of a sheath gas and sheath liq. Error anal. of the spectral data showed that the std. deviation in signal intensity for an analyte peak was less than ~ 5% over 3 h. The prodn. of stable electrosprays directly from microchip IEF device represents a step towards easily fabricated microanal. devices. Microchannel IEF sepns. of protein mixts. were demonstrated for uncoated polycarbonate microchips. Direct microchannel IEF-ESI-MS was demonstrated using the microfabricated chip with an ion-trap mass spectrometer for characterization of protein mixts.

L12 ANSWER 162 OF 277 CA COPYRIGHT 2002 ACS
AN 131:308438 CA
TI Microfabricated Polymer Devices for Automated Sample Delivery of Peptides for Analysis by Electrospray Ionization Tandem Mass Spectrometry
AU Chan, Jason H.; Timperman, Aaron T.; Qin, Dong; Aebersold, Ruedi
CS Department of Molecular Biotechnology, University of Washington, Seattle, WA, 98195, USA
SO Anal. Chem. (1999), 71(20), 4437-4444
AB Delivery of proteins and peptides to electrospray ionization mass spectrometers (ESI-MS) has been demonstrated using glass and quartz microfabricated devices. This paper reports the construction and use of poly(dimethylsiloxane) (PDMS) microfabricated soft polymer devices with mass spectrometry for protein anal. The PDMS devices were fabricated using replica molding against a patterned photoresist generated by photolithog. techniques. The PDMS devices were connected to the mass spectrometer via a derivatized transfer capillary and samples were transferred by electroosmotic pumping. The formulation of PDMS was optimized for compatibility with ESI, and the devices were tested for performance. The practical application of PDMS devices was demonstrated by the identification of rat serum albumin sepd. by 2-D gel electrophoresis. Extended contact of the sample with the surface of the PDMS device did not significantly affect the sample anal., and the limit of detection for samples run on a PDMS device was comparable to the limit of detection achieved on glass devices. This study suggests that PDMS devices fabricated using replica molding are compatible with ESI-MS. This will potentially lead to the construction of

inexpensive microfabricated devices with complex designs and advanced functionalities.

L12 ANSWER 169 OF 277 CA COPYRIGHT 2002 ACS
AN 131:254429 CA
TI Subattomole-Sensitivity Microchip Nanoelectrospray Source with Time-of-Flight Mass Spectrometry Detection
AU Lazar, Iulia M.; Ramsey, Roswitha S.; Sundberg, Steven; Ramsey, J. Michael
CS Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, 37831-6365, USA
SO Anal. Chem. (1999), 71(17), 3627-3631
AB A microfabricated microfluidic device coupled with a nanospray tip for electrospray ionization of dil. solns. is described. The device has been interfaced with a time-of-flight mass spectrometer and evaluated for sensitive, high-speed detection of peptides and proteins. The electrospray voltage was applied through the microchip to the nanospray capillary that was attached at the end of a microfabricated channel. Fluid delivery rates were 20-30 nL min-1 through the hybridized structure without any pressure assistance. Online microchip electrophoresis has been demonstrated and the effect of the capillary-chip junction on band broadening examd. Full mass spectra are acquired within 10-20 ms at 50-100 spectra s-1 storage rates. Detection of subattomole levels of sample from a 100 nM soln. is demonstrated for infusion expts.

L12 ANSWER 172 OF 277 CA COPYRIGHT 2002 ACS
AN 131:181768 CA
TI Microfabricated Devices for Capillary Electrophoresis-Electrospray Mass Spectrometry
AU Zhang, B.; Liu, H.; Karger, B. L.; Foret, F.
CS Barnett Institute and Department of Chemistry, Northeastern University, Boston, MA, 02115, USA
SO Anal. Chem. (1999), 71(15), 3258-3264
AB Two fundamental approaches for the coupling of microfabricated devices to electrospray mass spectrometry (ESI-MS) have been developed and evaluated. The microdevices, designed for electrophoretic sepn., were constructed from glass by std. photolithog./wet chem. etching techniques. Both approaches integrated sample inlet ports, preconcn. sample loops, the sepn. channel, and a port for ESI coupling. In one design, a modular, reusable microdevice was coupled to an external subatmospheric electrospray interface using a liq. junction and a fused silica transfer capillary. The transfer capillary allowed the use of an independent electrospray interface as well as fiber optic UV detection. In the second design, a miniaturized pneumatic nebulizer was fabricated as an integral part of the chip, resulting in a very simple device. The on-chip pneumatic nebulizer provided control of the flow of the electrosprayed liq. and minimized the dead vol. assocd. with droplet formation at the electrospray exit port. Thus, the microdevice substituted for a capillary electrophoresis instrument and an electrospray interface-traditionally two independent components. This type of microdevice is simple to fabricate and may thus be developed either as a part of a reusable system or as a disposable cartridge. Both devices were tested on CE sepns. of angiotensin peptides and a cytochrome c tryptic digest. Several electrolyte systems including a transient isotachophoretic preconcn. step were tested for sepn. and anal. by an ion trap mass spectrometer.

L12 ANSWER 173 OF 277 CA COPYRIGHT 2002 ACS
AN 131:181766 CA
TI Integration of Microfabricated Devices to Capillary

Electrophoresis-Electrospray Mass Spectrometry Using a Low Dead Volume Connection: Application to Rapid Analyses of Proteolytic Digests

AU Li, Jianjun; Thibault, Pierre; Bings, Nicolas H.; Skinner, Cameron D.; Wang, Can; Colyer, Christa; Harrison, Jed

CS Institute for Biological Sciences, Ottawa, ON, K1A 0R6, Can.

SO Anal. Chem. (1999), 71(15), 3036-3045

AB This report describes the development of a compact and versatile, micro-machined chip device enabling the efficient coupling of capillary electro-phoresis to electrospray mass spectrometry (CE-ESMS). On-chip sepn. provides a convenient means of achieving rapid sample cleanup and resoln. of multicomponent samples (typically 2-5 min) prior to mass spectral anal. A low dead vol. connection facilitating the coupling of microfabricated devices to CE-ESMS was evaluated using two different interfaces. The first configuration used disposable nanoelectrospray emitters directly coupled to the chip device via this low dead vol. junction, thereby providing rapid sepn. of complex protein digests. The performance of this interface was compared with that of more traditional configurations using a sheath flow CE-ESMS arrangement where a fused-silica capillary of varying length enabled further temporal resoln. of the multicomponent samples. The sensitivity and anal. characteristics of these interfaces were investigated in both neg. and pos. ion modes using std. peptide mixts. The sepn. performance for synthetic peptides using a chip coated with amine reagent ranged from 26 000 to 58 000 theor. plates for a sheath flow CE-ESMS interface comprising a 15-cm CE column. Replicate injections of a diln. series of peptide stds. provided detection limits of 45-400 nM without the use of online preconcn. devices. The reproducibility of migration time ranged from 0.9 to 1.5% RSD whereas RSDs of 5-10% were obsd. on peak areas. The application of these devices for the anal. of protein digests was further evaluated using online tandem mass spectrometry.

L12 ANSWER 174 OF 277 CA COPYRIGHT 2002 ACS

AN 131:153197 CA

TI Microfluidic devices connected to fused-silica capillaries with minimal dead volume

AU Bings, Nicolas H.; Wang, Can; Skinner, Cameron D.; Colyer, Christa L.; Thibault, Pierre; Harrison, D. Jed

CS Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2, Can.

SO Anal. Chem. (1999), 71(15), 3292-3296

AB Fused-silica capillaries were connected to microfluidic devices for capillary electrophoresis by drilling into the edge of the device using 200-μm tungsten carbide drills. The std. pointed drill bits create a hole with a conical-shaped bottom that leads to a geometric dead vol. of 0.7 nL at the junction, and significant band broadening when used with 0.2-nL sample plugs. The plate nos. obtained on the fused-silica capillary connected to the chip were ~16-25% of the predicted nos. The conical area was removed with a flat-tipped drill bit and the band broadening was substantially eliminated (on av. 98% of the predicted plate nos. were obsd.). All measurements were made while the device was operating with an electrospray from the end of the capillary. The effective dead vol. of the flat-bottom connection is minimal and allows microfluidic devices to be connected to a wide variety of external detectors.

L12 ANSWER 185 OF 277 CA COPYRIGHT 2002 ACS

AN 130:67359 CA

TI Rapid Prototyping of Microfluidic Systems in Poly(dimethylsiloxane)

AU Duffy, David C.; McDonald, J. Cooper; Schueller, Olivier J. A.; Whitesides, George M.

CS Department of Chemistry and Chemical Biology, Harvard University,

Cambridge, MA, 02138, USA
SO Anal. Chem. (1998), 70(23), 4974-4984
AB This paper describes a procedure that makes it possible to design and fabricate (including sealing) microfluidic systems in an elastomeric material-poly(dimethylsiloxane) (PDMS)-in less than 24 h. A network of microfluidic channels (with width >20 μm) is designed in a CAD program. This design is converted into a transparency by a high-resoln. printer; this transparency is used as a mask in photolithog. to create a master in pos. relief photoresist. PDMS cast against the master yields a polymeric replica contg. a network of channels. The surface of this replica, and that of a flat slab of PDMS, are oxidized in an oxygen plasma. These oxidized surfaces seal tightly and irreversibly when brought into conformal contact. Oxidized PDMS also seals irreversibly to other materials used in microfluidic systems, such as glass, silicon, silicon oxide, and oxidized polystyrene; a no. of substrates for devices are, therefore, practical options. Oxidn. of the PDMS has the addnl. advantage that it yields channels whose walls are neg. charged when in contact with neutral and basic aq. solns.; these channels support electroosmotic pumping and can be filled easily with liqs. with high surface energies (esp. water). The performance of microfluidic systems prepd. using this rapid prototyping technique has been evaluated by fabricating a miniaturized capillary electrophoresis system. Amino acids, charge ladders of pos. and neg. charged proteins, and DNA fragments were sepd. in aq. solns. with this system with resoln. comparable to that obtained using fused silica capillaries.

L12 ANSWER 186 OF 277 CA COPYRIGHT 2002 ACS
AN 130:63133 CA
TI Microfabricated device coupled with an electrospray ionization quadrupole time-of-flight mass spectrometer: protein identifications based on enhanced-resolution mass spectrometry and tandem mass spectrometry data
AU Figeys, Daniel; Lock, Chris; Taylor, Lorne; Aebersold, Ruedi
CS Institute for Marine Biosciences, National Research Council Canada, Halifax, NS, Can.
SO Rapid Commun. Mass Spectrom. (1998), 12(20), 1435-1444
AB We describe the coupling of a microfabricated fluidic device to an electrospray ionization (ESI) quadrupole time-of-flight mass spectrometer (QqTOFMS) for the identification of protein samples. The microfabricated devices consisted of three reservoirs connected via channels to a main capillary, which in turn was linked via a microspray interface to the QqTOFMS. Here we present preliminary results obtained using this system. Standardized solns. of myoglobin tryptic digest were analyzed indicating a limit of detection at the low to sub fmol/plL. The combination of the microfabricated device for rapid sample delivery and the rapid acquisition capability, enhanced resoln. and mass accuracy of the QqTOF offers unique possibilities for the rapid identification of proteins by database searching. This platform can generate MS data suitable for protein database searching by the peptide-mass fingerprinting approach and MS/MS data suitable for protein database searching. Here the results of the two database-searching approaches are compared and the possibilities of combining the two approaches for rapid identification of protein are discussed. Also, we present a comparison of the results obtained using the three-position microfabricated device coupled to the ESI-QqTOFMS and to an ESI-ion trap MS. Finally the combination of C-terminal 180 labeling of peptides and the microfabricated system for automated combined peptide-mass fingerprinting and sequence-tag database searching is discussed.

L12 ANSWER 193 OF 277 CA COPYRIGHT 2002 ACS

AN 129:267618 CA
TI A MEMS electrospray nozzle for mass spectroscopy
AU Desai, Amish; Tai, Yu-Chong; Davis, Michael T.; Lee, Terry D.
CS Department of Electrical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SO Transducers 97, Int. Conf. Solid-State Sens. Actuators (1997), Volume 2, 927-930 Publisher: Institute of Electrical and Electronics Engineers, New York, N. Y.
AB In this paper, we present our development of a micron-sized MEMS electrospray nozzle and demonstrate its application for electrospray mass spectroscopy (MS). The fabricated and tested micromachined electrospray nozzles are typically 40μm long and with 1-3 μm orifice diams. They also have built-in particle filters. This micromachined nozzle has been successfully interfaced with a mass spectrometer (Finnigan Mat LCQ Ion Trap) to perform std. characterization using a soln. of gramicidin S at a flow rate of 50 nL/min and a voltage potential of 4 kV. This MEMS nozzle has demonstrated valid MS analyses with lower flow rates, and it has many advantages over the traditional complex prepn. of a glass-capillary.

L12 ANSWER 195 OF 277 CA COPYRIGHT 2002 ACS
AN 129:242034 CA
TI An Integrated Microfluidics-Tandem Mass Spectrometry System for Automated Protein Analysis
AU Figeys, Daniel; Gygi, Steven P.; McKinnon, Graham; Aebersold, Ruedi
CS Institute for Marine Biosciences, National Research Council Canada, Halifax, NS, B3H 3Z1, Can.
SO Anal. Chem. (1998), 70(18), 3728-3734
AB We describe an integrated anal. system consisting of a microfluidics device micromachined using photolithog./etching technol., a panel of computer-controlled high-voltage relays, and an electrospray ionization tandem mass spectrometer. Movement of solvents and samples on the device and off the device to the mass spectrometer was achieved by directed electroosmotic pumping induced by the activation of a suitable constellation of high-voltage relays. The system was used for the sequential automated anal. of protein digests. We demonstrate low fentomole per μL sensitivity of detection and compatibility of the system with the automated anal. of proteins sepd. by two-dimensional gel electrophoresis.

L12 ANSWER 197 OF 277 CA COPYRIGHT 2002 ACS
AN 129:227593 CA
TI Nanoflow Solvent Gradient Delivery from a Microfabricated Device for Protein Identifications by Electrospray Ionization Mass Spectrometry
AU Figeys, Daniel; Aebersold, Ruedi
CS Department of Molecular Biotechnology, University of Washington, Seattle, WA, 98195-7730, USA
SO Anal. Chem. (1998), 70(18), 3721-3727
AB Microfabrication technol. offers the opportunity to construct microfluidic modules which are designed to perform specific, dedicated functions. Here we report the construction of a microfabricated device for the generation and delivery by electroosmotic pumping of solvent gradients at nanoliter per min flow rates. The device consists of three solvent reservoirs and channels which were etched in glass. Solvent gradients and solvent flows were generated by computer controlled differential electroosmotic pumping of aq. and org. phase, resp., from the solvent reservoirs. The device was integrated into an anal. system consisting of the solvent gradient delivery module, a reverse phase micro-column and an electrospray ionization ion trap mass spectrometer (MS). The system was used for the anal. at high sensitivity of peptides and peptide mixts. generated by proteolytic

digestion of proteins. We have measured an abs. limit of detection as low as 1 fmol and a concn. limit of detection at the 100 amol/μL level. The system was also successfully used for the identification of proteins sepd. by 1D and 2D gel electrophoresis. This was achieved by gradient frontal anal. of the peptide mixt. generated by proteolysis of the resp. proteins, and the automated generation and interpretation of collision-induced dissocn. spectra.

L12 ANSWER 198 OF 277 CA COPYRIGHT 2002 ACS
AN 129:227592 CA
TI A Microfabricated Dialysis Device for Sample Cleanup in Electrospray Ionization Mass Spectrometry
AU Xu, Naxing; Lin, Yuehe; Hofstadler, Steven A.; Matson, Dean; Call, Charles J.; Smith, Richard D.
CS Environmental Molecular Sciences Laboratory and Materials Resources Department, Pacific Northwest National Laboratory, Richland, WA, 99352, USA
SO Anal. Chem. (1998), 70(17), 3553-3556
AB A laser microfabricated device was constructed for rapid microdialysis cleanup of biol. samples for anal. by electrospray ionization mass spectrometry (ESI-MS) in both off-line and online modes. A microdialysis membrane was sandwiched between two chips having micromachined serpentine channels. The total vol. of the sample serpentine channel used for the microdialysis was 1 μL. Efficient desalting was demonstrated for both DNA and protein samples using ESI with an ion trap mass spectrometer after microdialysis against a counter flow of ESI-compatible buffer. Signal-to-noise ratios were also greatly enhanced compared to direct infusion of the original nondialyzed samples. Importantly, the microfabricated device allowed use of sample flow rates 1 order of magnitude smaller than previous designs based on a microdialysis fiber, allowing reduced sample utilization and improved sensitivity with ESI-MS. The effectiveness of the cleanup was attributed to the size difference between the sample channel and the buffer channel and the fact that the sample is continuously refreshed by the buffer counterflow. The results indicate substantial potential for construction of highly compact and rugged devices enabling field applications of ESI-MS.

L12 ANSWER 201 OF 277 CA COPYRIGHT 2002 ACS
AN 129:181903 CA
TI MEMS electrospray nozzle for mass spectroscopy
IN Tai, Yu-Chong; Desai, Amish; Lee, Terry; Davis, Mike
PA California Institute of Technology, USA
SO PCT Int. Appl., 28 pp.

PI	WO 9835376	A1	19980813	WO 1998-US1506	19980127
	US 5994696	A	19991130	US 1998-13961	19980127
PRAI	US 1997-36741P	P	19970127		

AB Microelectromech. system (MEMS) electrospray nozzles for mass spectroscopy comprise a channel field having an inner diam. between 0.3-3 μm; a nozzle tip; and a filter structure positioned on the channel field. Methods of fabricating the nozzles entailing etching of a sacrificial layer to form a microchannels are also described. HF.

L12 ANSWER 211 OF 277 CA COPYRIGHT 2002 ACS
AN 128:210879 CA
TI Polymer-based micromachining technology for microfluidic devices
IN Mastrangelo, Carlos H.; Man, Piu F.; Webster, James R.
PA Regents of the University of Michigan, USA; Mastrangelo, Carlos H.; Man, Piu F.; Webster, James R.
SO PCT Int. Appl., 43 pp.

PI WO 9807069 A1 19980219 WO 1997-US14054 19970811
PRAI US 1996-23393P P 19960812
AB The present invention relates to polymer-based micro-electro-mech. system (MEMS) technol. suitable for the fabrication of integrated microfluidic systems, particularly medical and chem. diagnostics system, ink-jet printer head, as well as any device that requires liq.- or gas-filled cavities for operation. The integrated microfluidic systems may consist of pumps, valves, channels, reservoirs cavities, reaction chambers, mixers, heaters, fluidic interconnects, diffusers, nozzles, and other microfluidic components on top of a regular circuit substrate. This technol. is vastly superior than any alternatives available such as glass-based, polysilicon-based MEMS technol. as well as hybrid "circuit board" technol. because of its simple construction low cost, low temp. processing, and its ability to integrate any electronic circuitry easily along with the fluidic parts.

L12 ANSWER 215 OF 277 CA COPYRIGHT 2002 ACS
AN 127:245007 CA
TI Integrated multichannel microchip electrospray ionization mass spectrometry: analysis of peptides from on-chip tryptic digestion of melittin
AU Xue, Qifeng; Dunayevskiy, Yuri M.; Foret, Frantisek; Karger, Barry L.
CS Dep. Chem., Barnett Inst., Northeastern Univ., Boston, MA, 02115, USA
SO Rapid Commun. Mass Spectrom. (1997), 11(12), 1253-1256
AB In continuation of our work to develop an integrated multichannel microchip interface to electrospray mass spectrometry (ESI-MS), this paper demonstrates one of several applications of this approach in monitoring tryptic digestion products. The multichannel microchip allowed integration of sample prepn. onto the microchip to facilitate the anal. process. Melittin was selected as a model oligopeptide because it possesses a cluster of four adjacent basic residues which enable probing the site specificity of trypsin as a function of digest times. Reactions were performed on-chip in different wells for specific time periods and then analyzed by infusion from the microchip by ESI-MS, using leucine-enkephalin as internal std. The rate of formation and disappearance of the mol. ion and individual fragments was followed for a melittin-to-trypsin concn. ratio of 300:1. The results indicate the potential of integrating enzymic reactions with multichannel microchip ESI-MS for automated optimization of reaction conditions while consuming only small amts. of sample.

L12 ANSWER 221 OF 277 CA COPYRIGHT 2002 ACS
AN 126:194637 CA
TI Generating Electrospray from Microchip Devices Using Electroosmotic Pumping
AU Ramsey, R. S.; Ramsey, J. M.
CS Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, 37831-6365, USA
SO Anal. Chem. (1997), 69(6), 1174-1178
AB A method of generating electrospray from solns. emerging from small channels etched on planar substrates is described. The fluids are delivered using electroosmotically induced pressures and are sprayed electrostatically from the terminus of a channel by applying an elec. potential of sufficient amplitude to generate the electrospray between the microchip and a conductor spaced from the channel terminus. No major modification of the microchip is required other than to expose a channel opening. The principles that regulate the fluid delivery are described and demonstrated. A spectrum for a test compd., tetrabutylammonium iodide, that was continuously electrophoresed was obtained by coupling the microchip to an ion trap mass spectrometer.

L12 ANSWER 222 OF 277 CA COPYRIGHT 2002 ACS
AN 126:86582 CA
TI Multichannel Microchip Electrospray Mass Spectrometry
AU Xue, Qifeng; Foret, Frantisek; Dunayevskiy, Yuriy M.; Zavracky, Paul M.; McGruer, Nicol E.; Karger, Barry L.
CS Barnett Institute and Department of Chemistry, Northeastern University, Boston, MA, 02115, USA
SO Anal. Chem. (1997), 69(3), 426-430
AB Microfabricated multiple-channel glass chips were successfully interfaced to an electrospray ionization mass spectrometer (ESI-MS). The microchip device was fabricated by std. photolithog., wet chem. etching, and thermal bonding procedures. A high voltage was applied individually from each buffer reservoir for spraying sample sequentially from each channel. With the orifice sampling of the MS grounded, it was found that a liq. flow of 100-200 nL/min was necessary to maintain a stable electrospray. The detection limit of the microchip MS expt. for myoglobin was found to be <6 × 10-8M. Samples in 75% methanol were successfully analyzed with good sensitivity, as were as aq. samples. The parallel multiple-channel microchip system allowed ESI-MS anal. of different samples of std. peptides and proteins in one chip.

L12 ANSWER 227 OF 277 CA COPYRIGHT 2002 ACS
AN 124:225418 CA
TI Instrumental Requirements for Nanoscale Liquid Chromatography
AU Chervet, J. P.; Ursem, M.; Salzmann, J. P.
CS LC Packings, Amsterdam, 1057 HM, Neth.
SO Anal. Chem. (1996), 68(9), 1507-12
AB Nanoscale liq. chromatog. (nano-LC), with packed columns of typically 75 μm i.d. × 15 cm length, packed with C18, 5 μm of stationary phase, and optimal flow rates of 180 nL/min, can be considered as a miniaturized version of conventional HPLC. Using the down-scaling factor, which corresponds to the ratio of the column diam. in square, (dconv/dmicro)2, excellent agreement between the theor. calcd. values and the values obtained using the down-scaling factor (~3800) has been obsd. This factor was applied to all system components, including flow rate, injection and detection vols., and connecting capillaries. Down-scaling of a conventional HPLC system to a nano-LC system is easy to realize in practice and involves using a micro-flow processor for nanoflow delivery (50-500 nL/min), a longitudinal nano-flow cell (≤3 nL), a microinjection valve (≤ 20 nL), low-dispersion con-necting tubing, and zero dead vol. connections. Excellent retention time reproducibility was measured with RSD values of ±0.1% for isocratic and ±0.2% for gradient elution. Plates counts of >100,000/m indicate the excellent performance of the entire nano-LC system. With minimal detect-able amts. of proteins in the low femtomole and sub-femtomole ranges (e.g., 520 amol for bovine serum albumin), high mass sensitivity was found, making nano-LC attractive for the microcharacterization of valuable and/or minute proteinaceous samples. Coupling nano-LC with concomitant mass spectrometry using nanoscale ion spray or electrospray interfaces looks very promising and is obviously the next step for future work.

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